

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

1-47. (Withdrawn)

48. (Currently Amended) An isolated nucleic acid, comprising a sequence of nucleotides that encodes SEQ ID NO: 43, ~~SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 69~~, or a complementary sequence of any of such nucleotides.

49-50. (Canceled)

51. (Currently Amended) An expression vector, comprising the isolated nucleic acid of claim 48 and a promoter, wherein the nucleic acid and the promoter are operably linked; ~~and operably linked to said nucleic acid, regulatory sequences effective for expression of the nucleic acid in a selected host cell.~~

52. (Original) The recombinant expression vector of claim 51, wherein said vector is suitable for transfection of a bacterial cell.

53. (Original) A heterologous cell transfected with the vector of claim 51, wherein said cell expresses a biologically active  $\beta$ -secretase.

54. (Original) The cell of claim 53, wherein said cell is a eukaryotic cell.

55. (Original) The cell of claim 53, wherein said cell is a bacterial cell.

56. (Original) The cell of claim 53, wherein said cell is an insect cell.

57. (Original) The cell of claim 53, wherein said cell is a yeast cell.

58. (Currently Amended) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of

nucleotides that encodes ~~SEQ ID NO: 2, SEQ ID NO: 43, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 74, SEQ ID NO: 75, a  $\beta$ -secretase protein,~~ or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

59. (Original) The method of claim 58, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

60. (Previously Amended) The method of claim 59, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

61. (Original) The method of claim 58, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

62. (Currently Amended) The method of claim 61, wherein said antibody binds specifically to ~~any of the protein compositions of SEQ ID NO: 2, SEQ ID NO: 43, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 74, SEQ ID NO: 75, or a  $\beta$ -secretase protein.~~

63. (Previously Amended) The method of claim 61, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

64. (Currently Amended) A heterologous cell, comprising

(i) a nucleic acid molecule encoding SEQ ID NO: 43, ~~SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 69,~~ or the complementary sequence of said nucleic acid molecule;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

65. (Original)) The cell of claim 64, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

66. (Previously Amended) The cell of claim 64, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

67. (Original) The cell of claim 64, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

68. (Previously Amended) The cell of claim 64, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

69. (Currently Amended) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is ~~selected from the group consisting of~~ SEQ ID NO: 82; ~~SEQ ID NO: 83;~~ ~~SEQ ID NO: 84;~~ ~~SEQ ID NO: 85;~~ ~~SEQ ID NO: 86;~~ ~~SEQ ID NO: 87;~~ ~~SEQ ID NO: 88;~~ ~~SEQ ID NO: 89;~~ ~~SEQ ID NO: 90;~~ ~~SEQ ID NO: 91;~~ ~~SEQ ID NO: 92;~~ ~~SEQ ID NO: 93;~~ ~~SEQ ID NO: 94;~~ ~~SEQ ID NO: 95;~~ and ~~SEQ ID NO: 96.~~

70-113. (Canceled)

114. (New) An isolated nucleic acid, comprising a sequence of nucleotides that encodes SEQ ID NO: 58 or a complementary sequence of any of such nucleotides.

115. (New) An expression vector, comprising the isolated nucleic acid of claim 114 and a promoter, wherein the nucleic acid and the promoter are operably linked.

116. (New) The expression vector of claim 115, wherein said vector is suitable for transfection of a bacterial cell.

117. (New) A heterologous cell transfected with the vector of claim 115, wherein said cell expresses a biologically active  $\beta$ -secretase.

118. (New) The cell of claim 117, wherein said cell is a eukaryotic cell.

119. (New) The cell of claim 117, wherein said cell is a bacterial cell.

120. (New) The cell of claim 117, wherein said cell is an insect cell.

121. (New) The cell of claim 117, wherein said cell is a yeast cell.

122. (New) An isolated nucleic acid, comprising a sequence of nucleotides that encodes SEQ ID NO: 59 or a complementary sequence of any of such nucleotides.

123. (New) An expression vector, comprising the isolated nucleic acid of claim 122 and a promoter, wherein the nucleic acid and the promoter are operably linked.

124. (New) The expression vector of claim 123, wherein said vector is suitable for transfection of a bacterial cell.

126. (New) A heterologous cell transfected with the vector of claim 123, wherein said cell expresses a biologically active  $\beta$ -secretase.

127. (New) The cell of claim 126, wherein said cell is a eukaryotic cell.

128. (New) The cell of claim 126, wherein said cell is a bacterial cell.

129. (New) The cell of claim 126, wherein said cell is an insect cell.

130. (New) The cell of claim 126, wherein said cell is a yeast cell.

131. (New) An isolated nucleic acid, comprising a sequence of nucleotides that encodes SEQ ID NO: 66 or a complementary sequence of any of such nucleotides.

132. (New) An expression vector, comprising the isolated nucleic acid of claim 131 and a promoter, wherein the nucleic acid and the promoter are operably linked.

133. (New) The expression vector of claim 132, wherein said vector is suitable for transfection of a bacterial cell.

134. (New) A heterologous cell transfected with the vector of claim 132, wherein said cell expresses a biologically active  $\beta$ -secretase.

135. (New) The cell of claim 134, wherein said cell is a eukaryotic cell.

136. (New) The cell of claim 134, wherein said cell is a bacterial cell.

137. (New) The cell of claim 134, wherein said cell is an insect cell.

138. (New) The cell of claim 134, wherein said cell is a yeast cell.

139. (New) An isolated nucleic acid, comprising a sequence of nucleotides that encodes SEQ ID NO: 67 or a complementary sequence of any of such nucleotides.

140. (New) An expression vector, comprising the isolated nucleic acid of claim 139 and a promoter, wherein the nucleic acid and the promoter are operably linked.

141. (New) The expression vector of claim 140, wherein said vector is suitable for transfection of a bacterial cell.

142. (New) A heterologous cell transfected with the vector of claim 140, wherein said cell expresses a biologically active  $\beta$ -secretase.

143. (New) The cell of claim 142, wherein said cell is a eukaryotic cell.

144. (New) The cell of claim 142, wherein said cell is a bacterial cell.

145. (New) The cell of claim 142, wherein said cell is an insect cell.

146. (New) The cell of claim 142, wherein said cell is a yeast cell.

147. (New) An isolated nucleic acid, comprising a sequence of nucleotides that encodes SEQ ID NO: 68 or a complementary sequence of any of such nucleotides.

148. (New) An expression vector, comprising the isolated nucleic acid of claim 147 and a promoter, wherein the nucleic acid and the promoter are operably linked.

149. (New) The expression vector of claim 148, wherein said vector is suitable for transfection of a bacterial cell.

150. (New) A heterologous cell transfected with the vector of claim 148, wherein said cell expresses a biologically active  $\beta$ -secretase.

151. (New) The cell of claim 150, wherein said cell is a eukaryotic cell.

152. (New) The cell of claim 150, wherein said cell is a bacterial cell.

153. (New) The cell of claim 150, wherein said cell is an insect cell.

154. (New) The cell of claim 150, wherein said cell is a yeast cell.

155. (New) An isolated nucleic acid, comprising a sequence of nucleotides that encodes SEQ ID NO: 69 or a complementary sequence of any of such nucleotides.

156. (New) An expression vector, comprising the isolated nucleic acid of claim 155 and a promoter, wherein the nucleic acid and the promoter are operably linked.

157. (New) The expression vector of claim 156, wherein said vector is suitable for transfection of a bacterial cell.

158. (New) A heterologous cell transfected with the vector of claim 156, wherein said cell expresses a biologically active  $\beta$ -secretase.

159. (New) The cell of claim 158, wherein said cell is a eukaryotic cell.

160. (New) The cell of claim 158, wherein said cell is a bacterial cell.

161. (New) The cell of claim 158, wherein said cell is an insect cell.

162. (New) The cell of claim 158, wherein said cell is a yeast cell.

163. (New) An isolated nucleic acid, comprising a sequence of nucleotides that encodes SEQ ID NO: 70 or a complementary sequence of any of such nucleotides.

164. (New) An expression vector, comprising the isolated nucleic acid of claim 163 and a promoter, wherein the nucleic acid and the promoter are operably linked.

165. (New) The expression vector of claim 163, wherein said vector is suitable for transfection of a bacterial cell.

166. (New) A heterologous cell transfected with the vector of claim 164, wherein said cell expresses a biologically active  $\beta$ -secretase.

167. (New) The cell of claim 166, wherein said cell is a eukaryotic cell.

168. (New) The cell of claim 166, wherein said cell is a bacterial cell.

169. (New) The cell of claim 166, wherein said cell is an insect cell.

170. (New) The cell of claim 166, wherein said cell is a yeast cell.

171. (New) An isolated nucleic acid, comprising a sequence of nucleotides that encodes SEQ ID NO: 74 or a complementary sequence of any of such nucleotides

172. (New) An expression vector, comprising the isolated nucleic acid of claim 171 and a promoter, wherein the nucleic acid and the promoter are operably linked.

173. (New) The expression vector of claim 172, wherein said vector is suitable for transfection of a bacterial cell.

174. (New) A heterologous cell transfected with the vector of claim 172, wherein said cell expresses a biologically active  $\beta$ -secretase.

175. (New) The cell of claim 174, wherein said cell is a eukaryotic cell.

176. (New) The cell of claim 174, wherein said cell is a bacterial cell.

177. (New) The cell of claim 174, wherein said cell is an insect cell.

178. (New) The cell of claim 174, wherein said cell is a yeast cell.

179. (New) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 58 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

180. (New) The method of claim 179, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

181. (Previously Amended) The method of claim 180, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

182. (New) The method of claim 179, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

183. (New) The method of claim 182, wherein said antibody binds specifically to SEQ ID NO: 58.

184. (New) The method of claim 182, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

185. (New) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 59 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

186. (New) The method of claim 185, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

187. (New) The method of claim 186, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

188. (New) The method of claim 185, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

189. (New) The method of claim 188, wherein said antibody binds specifically to SEQ ID NO: 59.



190. (New) The method of claim 188, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

191. (New) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 66 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

192. (New) The method of claim 191, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

193. (New) The method of claim 192, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

194. (New) The method of claim 191, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

195. (New) The method of claim 194, wherein said antibody binds specifically to SEQ ID NO: 66.

196. (New) The method of claim 194, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

197. (New) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 67 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

198. (New) The method of claim 197, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

199. (New) The method of claim 198, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

200. (New) The method of claim 197, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

201. (New) The method of claim 200, wherein said antibody binds specifically to SEQ ID NO: 67.

202. (New) The method of claim 197, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

203. (New) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 68 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

204. (New) The method of claim 203, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

205. (New) The method of claim 204, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

206. (New) The method of claim 203, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

207. (New) The method of claim 206, wherein said antibody binds specifically to SEQ ID NO: 68.

208. (New) The method of claim 206, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

209. (New) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 69 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

210. (New) The method of claim 209, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

211. (New) The method of claim 210, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

212. (New) The method of claim 211, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

213. (New) The method of claim 209, wherein said antibody binds specifically to SEQ ID NO: 69.

214. (New) The method of claim 212, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

215. (New) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 70 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

216. (New) The method of claim 215, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

217. (New) The method of claim 216, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

218. (New) The method of claim 215, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

219. (New) The method of claim 218, wherein said antibody binds specifically to SEQ ID NO: 70.

220. (New) The method of claim 218, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

221. (New) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell transfected with a vector comprising a sequence of nucleotides that encodes SEQ ID NO: 74 or a complementary sequence of such nucleotides under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

222. (New) The method of claim 221, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.

223. (New) The method of claim 222, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

224. (New) The method of claim 221, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.

225. (New) The method of claim 224, wherein said antibody binds specifically to SEQ ID NO: 74.

226. (New) The method of claim 221, wherein said antibody further lacks significant immunoreactivity with a protein having the sequence of SEQ ID NO: 2.

227. (New) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

228. (New) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.
229. (New) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.
230. (New) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.
231. (New) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.
232. (New) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.
233. (New) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.
234. (New) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.
235. (New) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.
236. (New) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.
237. (New) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.
238. (New) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.
239. (New) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

240. (New) The cell of claim 67, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

241. (New) A heterologous cell, comprising

(i) a nucleic acid molecule encoding SEQ ID NO: 58 or the complementary sequence of said nucleic acid molecule;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

242. (New) The cell of claim 241, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

243. (New) The cell of claim 241, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

244. (New) The cell of claim 241, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

245. (New) The cell of claim 241, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

246. (New) The cell of claim 244, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

247. (New) The cell of claim 244, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

248. (New) The cell of claim 244, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

249. (New) The cell of claim 244, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

250. (New) The cell of claim 244, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

251. (New) The cell of claim 244, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

252. (New) The cell of claim 244, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

253. (New) The cell of claim 244, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

254. (New) The cell of claim 244, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

255. (New) The cell of claim 244, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

256. (New) The cell of claim 244, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

257. (New) The cell of claim 244, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

258. (New) The cell of claim 244, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

259. (New) The cell of claim 244, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

260. (New) A heterologous cell, comprising

(i) a nucleic acid molecule encoding SEQ ID NO: 59 or the complementary sequence of said nucleic acid molecule;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

261. (New) The cell of claim 260, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

262. (New) The cell of claim 260, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

263. (New) The cell of claim 260, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

264. (New) The cell of claim 260, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).



265. (New) The cell of claim 263, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

266. (New) The cell of claim 263, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

267. (New) The cell of claim 263, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

268. (New) The cell of claim 263, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

269. (New) The cell of claim 263, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

270. (New) The cell of claim 263, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

271. (New) The cell of claim 263, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

272. (New) The cell of claim 263, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

273. (New) The cell of claim 263, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

274. (New) The cell of claim 263, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

275. (New) The cell of claim 263, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

276. (New) The cell of claim 263, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

277. (New) The cell of claim 263, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

278. (New) The cell of claim 263, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

279. (New) A heterologous cell, comprising

(i) a nucleic acid molecule encoding SEQ ID NO: 66 or the complementary sequence of said nucleic acid molecule;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

280. (New) The cell of claim 279, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

281. (New) The cell of claim 279, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

282. (New) The cell of claim 279, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

283. (New) The cell of claim 279, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54

(MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

284. (New) The cell of claim 282, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

285. (New) The cell of claim 282, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

286. (New) The cell of claim 282, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

287. (New) The cell of claim 282, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

288. (New) The cell of claim 282, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

289. (New) The cell of claim 282, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

290. (New) The cell of claim 282, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

291. (New) The cell of claim 282, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

292. (New) The cell of claim 282, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

293. (New) The cell of claim 282, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

294. (New) The cell of claim 282, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

295. (New) The cell of claim 282, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

296. (New) The cell of claim 282, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

297. (New) The cell of claim 282, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

298. (New) A heterologous cell, comprising

(i) a nucleic acid molecule encoding SEQ ID NO: 67 or the complementary sequence of said nucleic acid molecule;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

299. (New) The cell of claim 298, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

300. (New) The cell of claim 298, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

301. (New) The cell of claim 298, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

302. (New) The cell of claim 298, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

303. (New) The cell of claim 301, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

304. (New) The cell of claim 301, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

305. (New) The cell of claim 301, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

306. (New) The cell of claim 301, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

307. (New) The cell of claim 301, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

308. (New) The cell of claim 301, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

309. (New) The cell of claim 301, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

310. (New) The cell of claim 301, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

311. (New) The cell of claim 301, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

312. (New) The cell of claim 301, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

313. (New) The cell of claim 301, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

312. (New) The cell of claim 301, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

313. (New) The cell of claim 301, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

314. (New) The cell of claim 301, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

315. (New) A heterologous cell, comprising

(i) a nucleic acid molecule encoding SEQ ID NO: 68 or the complementary sequence of said nucleic acid molecule;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

316. (New) The cell of claim 315, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

317. (New) The cell of claim 315, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

318. (New) The cell of claim 315, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

319. (New) The cell of claim 315, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

320. (New) The cell of claim 318, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

321. (New) The cell of claim 318, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

322. (New) The cell of claim 318, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

323. (New) The cell of claim 318, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

324. (New) The cell of claim 318, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

325. (New) The cell of claim 318, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

326. (New) The cell of claim 318, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

327. (New) The cell of claim 318, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

328. (New) The cell of claim 318, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

329. (New) The cell of claim 318, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

330. (New) The cell of claim 318, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

331. (New) The cell of claim 318, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

332. (New) The cell of claim 318, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

333. (New) The cell of claim 318, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

334. (New) A heterologous cell, comprising

(i) a nucleic acid molecule encoding SEQ ID NO: 69 or the complementary sequence of said nucleic acid molecule;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

335. (New) The cell of claim 334, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

336. (New) The cell of claim 334, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.



337. (New) The cell of claim 334, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

338. (New) The cell of claim 334, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

339. (New) The cell of claim 337, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

340. (New) The cell of claim 337, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

341. (New) The cell of claim 337, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

342. (New) The cell of claim 337, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

343. (New) The cell of claim 337, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

344. (New) The cell of claim 337, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

345. (New) The cell of claim 337, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

346. (New) The cell of claim 337, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

347. (New) The cell of claim 337, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

348. (New) The cell of claim 337, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

349. (New) The cell of claim 337, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

350. (New) The cell of claim 337, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

351. (New) The cell of claim 337, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

352. (New) The cell of claim 337, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

353. (New) A heterologous cell, comprising

(i) a nucleic acid molecule encoding SEQ ID NO: 70 or the complementary sequence of said nucleic acid molecule;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

354. (New) The cell of claim 353, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

355. (New) The cell of claim 353, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

356. (New) The cell of claim 353, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

357. (New) The cell of claim 353, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

358. (New) The cell of claim 356, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

359. (New) The cell of claim 356, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

360. (New) The cell of claim 356, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

361. (New) The cell of claim 356, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

362. (New) The cell of claim 356, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

363. (New) The cell of claim 356, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

364. (New) The cell of claim 356, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

365. (New) The cell of claim 356, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

366. (New) The cell of claim 356, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.

367. (New) The cell of claim 356, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.

368. (New) The cell of claim 356, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.

369. (New) The cell of claim 356, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.

370. (New) The cell of claim 356, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.

371. (New) The cell of claim 356, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.

372. (New) A heterologous cell, comprising

(i) a nucleic acid molecule encoding SEQ ID NO: 74 or the complementary sequence of said nucleic acid molecule;

(ii) a nucleic acid molecule encoding a  $\beta$ -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

373. (New) The cell of claim 372, wherein said nucleic acid encoding said  $\beta$ -secretase protein is heterologous to said cell.

374. (New) The cell of claim 372, wherein both said nucleic acids encoding said  $\beta$ -secretase protein and encoding said  $\beta$ -secretase substrate molecule are heterologous to said cell.

375. (New) The cell of claim 372, wherein said  $\beta$ -secretase substrate molecule is selected from the group consisting of APPwt, APPsw, and  $\beta$ -secretase cleavable fragments thereof.

376. (New) The cell of claim 372, wherein said  $\beta$ -secretase substrate is selected from the group consisting of a maltose binding protein fused at the carboxy-terminus to the 125 carboxyl-terminal amino acids of APP having the cleavage site of SEQ ID NO: 54 (MBP-C125wt) and a maltose binding protein fused at the carboxy-terminus to the 125 C-terminus amino acids of APP having the cleavage site of SEQ ID NO: 51 (MBP-C125sw).

377. (New) The cell of claim 375, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 83.

378. (New) The cell of claim 375, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 84.

379. (New) The cell of claim 375, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 85.

380. (New) The cell of claim 375, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 86.

381. (New) The cell of claim 375, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 87.

382. (New) The cell of claim 375, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 88.

383. (New) The cell of claim 375, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 89.

384. (New) The cell of claim 375, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 90.

385. (New) The cell of claim 375, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 91.
386. (New) The cell of claim 375, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 92.
387. (New) The cell of claim 375, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 93.
388. (New) The cell of claim 375, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 94.
389. (New) The cell of claim 375, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 95.
390. (New) The cell of claim 375, wherein said  $\beta$ -secretase-cleavable fragment is SEQ ID NO: 96.